

Amendments to the Claims

Please amend claims 1-4, 14 and 25-26 as indicated in the listing of claims.

Claims 10 and 35 were previously cancelled without prejudice. Claims 13, 17, 20-24, 28 and 47-72 were previously withdrawn.

The listing of claims will replace all prior versions, and listings of claims in the application.

Listing of Claims:

1. (Currently amended) A method for detecting liver damage due to hepatitis infection in a subject, said method comprising contacting a sample from the subject with a plasma ~~kallikrein-like~~ kallikrein peptidase detection reagent, wherein the ~~kallikrein-like~~ kallikrein peptidase detection reagent detects the ~~kallikrein-like~~ kallikrein peptidase, and wherein interaction of the ~~kallikrein-like~~ kallikrein peptidase with the ~~kallikrein-like~~ kallikrein peptidase detection reagent is indicative of liver damage due to hepatitis infection in the subject.
2. (Currently amended) The method of claim 1, wherein the ~~kallikrein-like~~ kallikrein peptidase is plasma kallikrein.
3. (Currently amended) The method of claim 1, wherein the ~~kallikrein-like~~ kallikrein peptidase detection reagent is a substrate cleaved by kallikrein.
4. (Currently amended) The method of claim 1, wherein the ~~kallikrein-like~~ kallikrein peptidase detection reagent is a kallikrein binding reagent.
5. (Original) The method of claim 2, further comprising contacting the sample with an alpha-2-macroglobulin detection reagent.

6. (Original) The method of claim 5, wherein kallikrein detected by the method is bound to alpha-2-macroglobulin.
7. (Original) The method of claim 1, wherein first sample is a blood or a plasma sample.
8. (Original) The method of claim 1, wherein the subject is a mammal.
9. (Original) The method of claim 1, wherein the subject is a stable liver transplant patient.
10. (Canceled).
11. (Original) The method of claim 1, wherein the subject has an HCV infection.
12. (Original) The method of claim 1, wherein the subject has a recurrent HCV infection.
13. (Withdrawn) The method of claim 1, wherein the subject has an HBV infection.
14. (Currently amended) The method of claim 1, wherein the ~~kallikrein-like~~ kallikrein peptidase detection reagent comprises a peptide.
15. (Original) The method of claim 1, further comprising detecting C3a, C4a, or a combination thereof.

16. (Original) The method of claim 1, wherein the subject has a liver disease selected from liver abscess, liver cancer, either primary or metastatic, cirrhosis, such as cirrhosis caused by the alcohol consumption or primary biliary cirrhosis, amebic liver abscess, autoimmune hepatitis, biliary atresia, coccidioidomycosis disseminated, delta agent (hepatitis d), hemochromatosis, hepatitis a, hepatitis b, hepatitis c, or other hepatitis virus, hepatocellular carcinoma, pyogenic liver abscess, Reye's syndrome, sclerosing cholangitis, Wilson's disease, drug induced hepatotoxicity, or fulminant or acute liver failure.

17. (Withdrawn) The method of claim 15, further comprising detecting interaction of the C4a detection reagent with C4a, wherein an elevated level of C4a indicates autoimmune liver damage.

18. (Original) The method of claim 2, wherein the method further comprises:
dividing the sample into a first portion and a second portion before contacting the sample with the substrate;
adding a kallikrein protease inhibitor to the first portion of the sample before contacting the sample with the substrate; and
comparing substrate cleavage in the first portion with substrate cleavage in the second portion, wherein a difference in substrate cleavage is indicative of liver damage.

19. (Original) The method of claim 18, wherein the kallikrein protease inhibitor is PPACK II.

20. (Withdrawn) The method of claim 1, further comprising contacting the sample with a prekallikrein detection reagent and detecting interaction of the prekallikrein with the prekallikrein detection reagent, wherein a difference in the level of the prekallikrein is indicative of liver damage in the subject.

21. (Withdrawn) The method of claim 4, wherein the kallikrein binding reagent comprises an anti-kallikrein antibody or an active site reactive reagent.

22. (Withdrawn) A kit comprising a first container containing a kallikrein-like peptidase detection reagent.

23. (Withdrawn) A kit comprising a first container containing a kallikrein-like peptidase detection reagent and a second container containing an alpha-2-macroglobulin detection reagent.

24. (Withdrawn) A kit comprising a first container containing a kallikrein-like peptidase detection reagent and a second container containing a C4a detection reagent or a C3a detection reagent, or a combination thereof.

25. (Currently amended) A method for monitoring the progression of liver damage due to hepatitis infection in a subject comprising:

contacting a first sample and a second sample with a ~~kallikrein-like~~ kallikrein peptidase detection reagent, wherein the first sample is from a first timepoint and the second sample is from a second timepoint, and wherein the kallikrein-like peptidase detection reagent detects kallikrein-like peptidase; and

comparing the level of ~~kallikrein-like~~ kallikrein peptidase in the first sample and the second sample, wherein a change in the relative quantity of the ~~kallikrein-like~~ kallikrein peptidase is indicative of a change in liver damage state.

26. (Currently amended) The method of claim 25, wherein the ~~kallikrein-like~~ kallikrein peptidase is kallikrein.

27. (Original) The method of claim 26, further comprising contacting the sample with a plasma peptidase or protease inhibitor detection reagent.

28. (Original) The method of claim 27, wherein the inhibitor is alpha-2-macroglobulin, C1 inhibitor or alpha-1 antitrypsin inhibitor or antithrombin.

29. (Original) The method of claim 28, wherein kallikrein measured by the method is bound to alpha-2-macroglobulin.

30. (Original) The method of claim 25, wherein the first sample and the second sample are plasma or a blood sample.

31. (Original) The method of claim 25, wherein the subject is a mammal.

32. (Original) The method of claim 25, wherein the subject is a human.

33. (Original) The method of claim 25, wherein the subject is a stable liver transplant patient.

34. (Original) The method of claim 26, wherein the subject is a stable liver transplant patient.

35. (Canceled).

36. (Original) The method of claim 35, wherein the subject has an HCV infection.

37. (Original) The method of claim 35, wherein the subject has a recurrent HCV infection.
38. (Withdrawn) The method of claim 35, wherein the subject has an HBV infection.
39. (Original) The method of claim 25, further comprising contacting the first sample and the second sample with a C3a and a C4a detection reagent.
40. (Original) The method of claim 39, further comprising determining a relative quantity of C3a and C4a by detecting the amount of interaction of the C3a and C4a detection reagent with C3a and C4a, respectively.
41. (Original) A method for detecting kallikrein in a sample, said method comprising contacting the sample with an isolated tri, tetra or penta peptide containing an arginine residue at the P1 position, wherein the peptide comprises a peptidase substrate.
42. (Original) The method of claim 41, wherein the peptide further comprises a detectable moiety.
43. (Original) The method of claim 42, wherein the detectable moiety is an enzyme, radioisotope, fluorescent compound, colloidal metal, a chromogenic moiety, chemiluminescent compound, phosphorescent compound, or bioluminescent compound.
44. (Original) The method of claim 43, wherein the chromogenic moiety is pNA.
45. (Original) The method of claim 41, wherein the sample is a blood-based sample.

46. (Original) The method of claim 41, wherein the blood-based sample is a plasma sample.

47. (Withdrawn) A method for determining toxicity of a therapeutic agent in a subject comprising contacting a sample from the subject with a kallikrein-like peptidase detection reagent and determining a kallikrein-like peptidase level in the sample, wherein an elevated kallikrein-like peptidase level indicates toxicity of the therapeutic agent.

48. (Withdrawn) The method of claim 47, wherein the elevated kallikrein-like peptidase level is determined by comparing the kallikrein-like peptidase level of the sample with a kallikrein-like peptidase level of a control not containing kallikrein-like peptidase.

49. (Withdrawn) The method of claim 47, wherein the kallikrein-like peptidase is kallikrein.

50. (Withdrawn) The method of claim 47, wherein the kallikrein-like peptidase detection reagent is a substrate cleaved by kallikrein.

51. (Withdrawn) The method of claim 47, wherein the kallikrein-like peptidase detection reagent is a kallikrein binding reagent.

52. (Withdrawn) The method of claim 47, wherein the kallikrein binding reagent comprises an anti-kallikrein antibody.

53. (Withdrawn) The method of claim 47, further comprising contacting the sample with an alpha-2-macroglobulin detection reagent.

54. (Withdrawn) The method of claim 53, wherein kallikrein is bound to alpha-2-macroglobulin, C1 inhibitor, antithrombin or alpha 1 antitrypsin inhibitor.

55. (Withdrawn) The method of claim 47, wherein the first sample is a blood or plasma sample.

56. (Withdrawn) The method of claim 47, wherein the subject is a mammal.

57. (Withdrawn) A method for detecting liver damage in a subject, said method comprising contacting a sample from the subject with a series of detection reagents that are specific for each member of a liver damage panel comprising kallikrein, wherein an elevated level of one or more members of the liver damage panel is indicative of liver damage in the subject.

58. (Withdrawn) The method of claim 57, wherein the liver damage panel comprises complement components.

59. (Withdrawn) The method of claim 58, wherein the liver damage panel further comprises a mannan binding serine protease, C1 esterase, serum amyloid protein, and C-reactive protein.

60. (Withdrawn) The method of claim 59, wherein the complement components include C3a and C4a.

61. (Withdrawn) The method of claim 60 wherein the complement components further include activated mannan binding serine protease-1.

62. (Withdrawn) An *in vitro* method for screening a therapeutic agent for toxicity, said method comprising:

incubating a liver cell cultured in cell culture medium with the therapeutic compound to obtain sample cell culture medium;

contacting the sample cell culture medium with a kallikrein-like peptidase detection reagent, wherein interaction of the kallikrein-like peptidase with the kallikrein-like peptidase detection agent is indicative of therapeutic agent toxicity.

63. (Withdrawn) The method of claim 62, wherein the kallikrein-like peptidase is kallikrein.

64. (Withdrawn) The method of claim 65, wherein the kallikrein-like peptidase detection reagent is a substrate cleaved by kallikrein.

65. (Withdrawn) The method of claim 65, wherein the kallikrein-like peptidase detection reagent is a kallikrein binding reagent.

66. (Withdrawn) The method of claim 65, wherein the kallikrein binding reagent comprises an anti-kallikrein antibody.

67. (Withdrawn) The method of claim 63, further comprising contacting the sample with an alpha-2-macroglobulin, C1 inhibitor, antithrombin or alpha-1 antitrypsin detection reagent.

68. (Withdrawn) The method of claim 67, wherein kallikrein detected by the method is bound to alpha-2-macroglobulin, C1 inhibitor, antithrombin or alpha-1 antitrypsin.

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69. (Withdrawn) The method of claim 2, further comprising contacting the sample with a C1 inhibitor detection reagent.

70. (Withdrawn) The method of claim 2, further comprising contacting the sample with a alpha 1 antitrypsin detection reagent.

71. (Withdrawn) The method of claim 2, further comprising contacting the sample with a antithrombin detection reagent.

72. (Withdrawn) The method of claim 42, wherein the detectable moiety is an antibody that detects the action of kallikrein on a peptide substrate.